

AMENDMENTS TO THE SPECIFICATION

Please amend the specification as follows:

Replace the paragraph on page 158, lines 7-20 with the following:

Nucleic acid encoding each the MTSP7 or protease domain thereof was cloned (with a C313S mutation into a derivative, modified by removal of a restriction site as described below, of the *Pichia Pastoris* vector pPIC9K (available from Invitrogen; see SEQ ID NO. 45). Plasmid ~~pPIC9K~~ pPIC9K features include the 5' AOX1 promoter fragment at 1-948; 5' AOX1 primer site at 855-875; alpha-factor secretion signal(s) at 949-1218; 3' AOX1 primer site at 1327-1347; 3' AOX1 transcription termination region at 1253-1586; HIS4 ORF at 4514-1980; kanamycin resistance gene at 5743-4928; 3' AOX1 fragment at 6122-6879; ColE1 origin at 7961-7288; and the ampicillin resistance gene at 8966-8106. The plasmid used herein is derived from pPIC9K by eliminating the XhoI site in the kanamycin resistance gene and the resulting vector is herein designated pPIC9KX.

Replace the paragraph on page 9, line 29 through page 10, line 3 with the following:

In one embodiment, the isolated nucleic acid fragment hybridizes to a nucleic acid molecule containing the nucleotide sequence set forth in SEQ ID No: 15 or 17 (or degenerates thereof) under high stringency conditions, in ~~one~~ other embodiments the isolated nucleic acid fragment contains the sequence of nucleotides set forth in ~~any of~~ SEQ ID Nos. ~~[[15-18.]]~~ 15 or 17. A full-length MTSP7 is set forth in SEQ ID No. ~~[[18]]~~ 16 and is encoded by SEQ ID No. ~~[[17]]~~ 15 or degenerates thereof.

Replace the paragraph on page 19, lines 1-21 with the following:

The MTSP7 protein, with the protease domains indicated, is illustrated in Figure 1. Smaller portions thereof that retain protease activity are contemplated. The protease domains from MTSPs vary in size and constitution, including insertions and deletions in surface loops. They retain conserved structure, including at least one of the active site triad (see, *e.g.*, the catalytic triad of the MTSP in SEQ ID No. 16 is H₂₄₈, D₂₉₃, S₃₈₉), primary specificity pocket, oxyanion hole and/or other features of serine protease domains of proteases. Thus, for purposes herein, the protease domain is a portion of a MTSP, as defined herein, and is homologous to a domain of other MTSPs, such as corin, enteropeptidase, human airway trypsin-like protease (HAT), MTSP1, TMPRSS2, and TMPRSS4, which have

been previously identified; it was not recognized, however, that an isolated single chain form of the protease domain could function proteolytically in *in vitro* assays. As with the larger class of enzymes of the chymotrypsin (S1) fold (see, *e.g.*, Internet accessible MEROPS data base), the MTSPs protease domains share a high degree of amino acid sequence identity. The His, Asp and Ser residues necessary for activity are present in conserved motifs. The activation site, which results in the N-terminus of second chain in the two chain ~~forms~~ ~~is has~~ forms, has a conserved motif and readily can be identified (see, *e.g.*, amino acids [[2-6]] 206-208).

Replace the paragraph on page 20, lines 4-16 with the following:

As used herein an MTSP7, whenever referenced herein, includes at least one or all of or any combination of:

a polypeptide encoded by the sequence of nucleotides set forth in SEQ ID No. 15;

a polypeptide encoded by a sequence of nucleotides that hybridizes under conditions of low, moderate or high stringency to the sequence of nucleotides set forth in SEQ ID No. 15;

a polypeptide that comprises the sequence of amino acids set forth as amino acids 206-438 of SEQ ID No. 16;

a polypeptide that comprises a sequence of amino acids having at least about 60%, 70%, 80%, 85%, 90% or 95% sequence identity with the sequence of amino acids set forth in SEQ ID No. 16 or [[17;]] 18; and/or

a splice variant of the MTSP7 set forth in SEQ ID No. 15.

Replace the paragraph on page 32, lines 33-37 with the following:

As used herein, a probe or primer based on a nucleotide sequence disclosed herein, includes at least 10, 14, generally at least 16 or 30 or 100 contiguous sequence of nucleotides of SEQ ID No. 15, except for a region that includes the sequence that encodes amino acids 117-171 and 185-354 of SEQ ID [[Nos. 15 and]] No. 16.

Replace the paragraph on page 54, lines 12-26 with the following:

In certain embodiments, the isolated nucleic acid fragment hybridizes to the nucleic acid having the nucleotide sequence set forth in SEQ ID No: 15 (or the molecules in the figure in the FIGURE) under high stringency conditions, and generally contains the sequence

of nucleotides set forth in SEQ ID Nos. [[15-17;]] 15 or 17; see also the Figure). The protein contains a transmembrane domain (TM), a SEA domain and a serine protease domain.

Muteins of the protein are also provided in which amino acids are replaced with conservative amino acids. Among the muteins are those in which the Cys residues, is/are replaced with generally conservative amino acid residues, such as a serine. Such muteins are also provided herein. Each of such domains is provided herein as are nucleic acid molecules that include sequences of nucleotides encoding such domains. Some MTSPs can additionally include a LDLR domain, a scavenger-receptor cysteine rich (SRCR) domain and other domains.

Replace the paragraph on page 75, line 28 through page 76, line 6 with the following:

For example, in practicing such methods the MTSP7 polypeptide is mixed with a potential binding partner or an extract or fraction of a cell under conditions that allow the association of potential binding partners with the polypeptide. After mixing, peptides, polypeptides, proteins or other molecules that have become associated with an MTSP7 are separated from the mixture. The binding partner that bound to the MTSP7 then can be removed and further analyzed. To identify and isolate a binding partner, the entire protein, for instance the entire disclosed protein of SEQ ID Nos. [[15 or 17]] 16 or 18 can be used. Alternatively, a fragment of the protein can be used.

Replace the paragraph on page 79, line 24 through page 80, line 14 with the following:

Hybridization conditions are modified using known methods (see, *e.g.*, Sambrook *et al.* (1989) MOLECULAR CLONING: A LABORATORY MANUAL, 2nd Ed. Cold Spring Harbor Laboratory Press); and Ausubel *et al.* (1995) CURRENT PROTOCOLS IN MOLECULAR BIOLOGY, Greene Publishing Co., NY), as required for each probe.

Hybridization of total cellular RNA or RNA enriched for polyA RNA can be accomplished in any available format. For instance, total cellular RNA or RNA enriched for polyA RNA can be affixed to a solid support, and the solid support exposed to at least one probe comprising at least one, or part of one of the nucleic acid molecules under conditions in which the probe will specifically hybridize. Alternatively, nucleic acid fragments comprising at least one, or part of one of the sequences can be affixed to a solid support, such as a porous glass wafer. The glass wafer then can be exposed to total cellular RNA or polyA RNA from a sample under conditions in which the affixed sequences will specifically hybridize. Such glass wafers and hybridization methods are widely available, for example, those disclosed by

Beattie (WO 95/11755). By examining for the ability of a given probe to specifically hybridize to an RNA sample from an untreated cell population and from a cell population exposed to the agent, agents which up or down regulate the expression of a nucleic acid encoding the protein having the sequence set forth in any of SEQ ID Nos. [[15-18,]] 16 and 18, particularly 18, are identified.